Interactions of Chemical Mechanical Planarization Nanoparticles with Model Cell Membranes: Implications for Nanoparticle Toxicity (425.041)

PI:

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- Khanh An Huynh, PhD, DoGEE, JHU – currently a NRC research fellow at EPA
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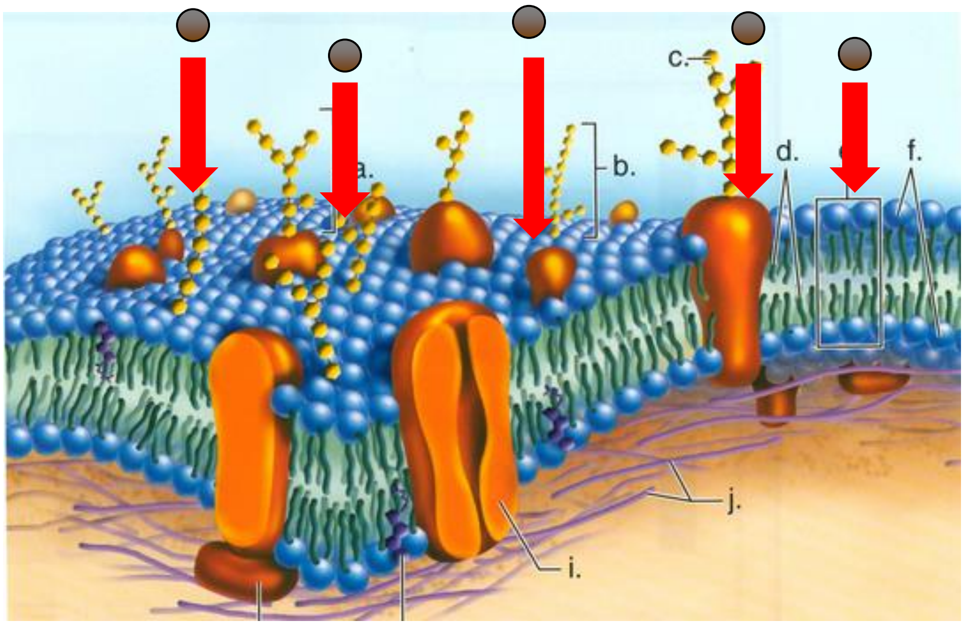
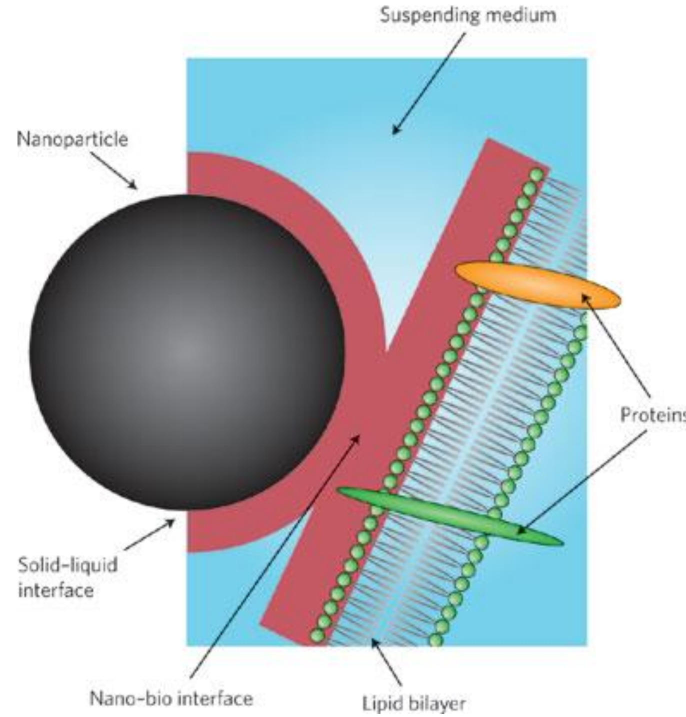
Cost Share (other than core ERC funding):

- $101,472 from Johns Hopkins University in the form of 80% of tuition for 3 years

Objectives





- **To investigate the propensity of chemical mechanical planarization nanoparticles (silica, ceria, and alumina) to attach to model biological membranes**
- **To develop a rapid assay to assess the propensity of nanomaterials to absorb on biological membranes**

Sylvia S. Mader, *Biology,* 9th ed., 2007, McGraw-Hill.   Nel et al., *Nature Materials* 2009, 8, 543–557.

ESH Metrics and Impact

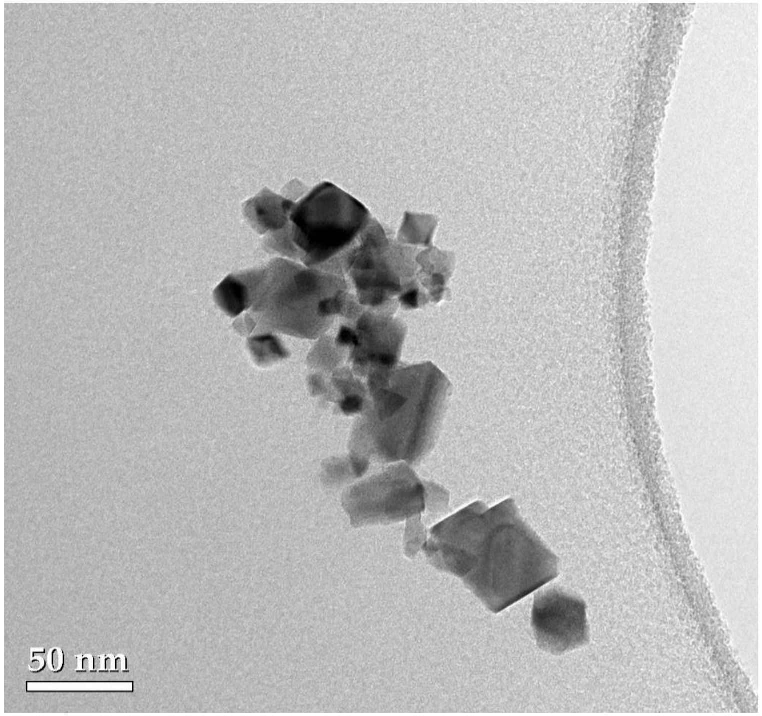
1. **Rapid assay for propensity of CMP particles to bind to cell membranes**
   - **Use of sensitive quartz crystal microbalance (QCM-D)**
2. **Reduction in the use of CMP particles that bind strongly to membranes**
   - **CMP particles will be tested with binding assay before being employed in semiconductor fabrication plants**
3. **Reduction in emission of CMP particles that bind strongly to membranes to environment**
   - **CMP nanoparticles may be replaced with other alternative materials/particles that do not strongly interact with biological membranes**

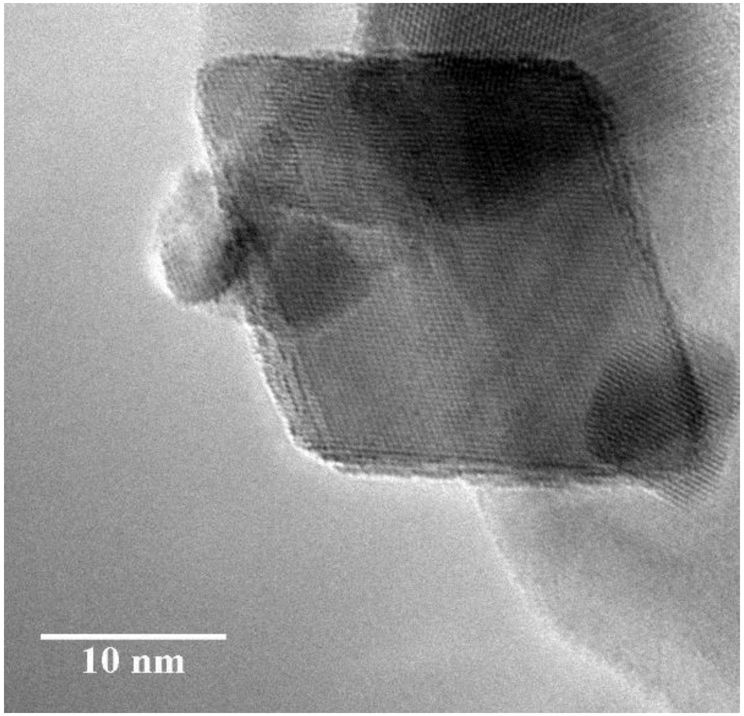
Chemical Mechanical Planarization Particles

http://www.levitronix.com/cmp-slurry.html

- **CeO_2, Al_2O_3, and SiO_2 nanoparticles are employed in large amounts for chemical mechanical planarization**

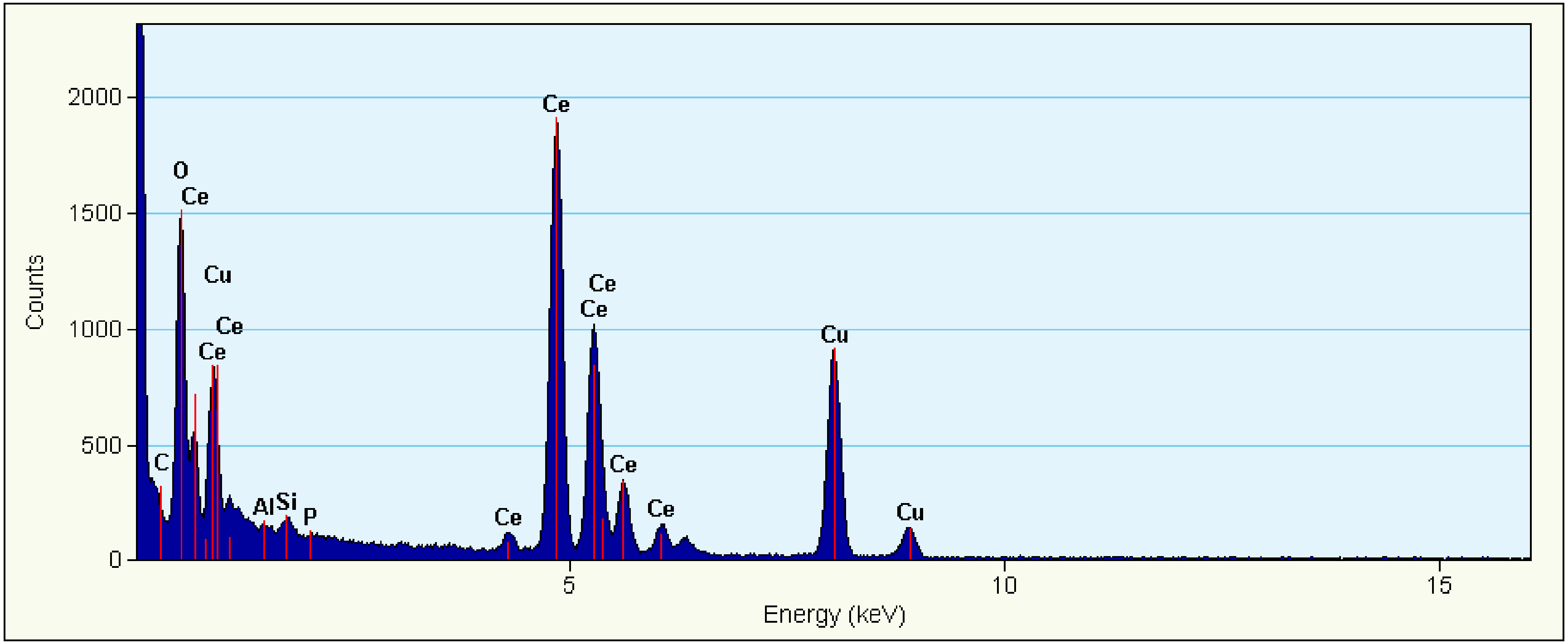
Characterization of CeO_2 NPs from Sierra's Lab





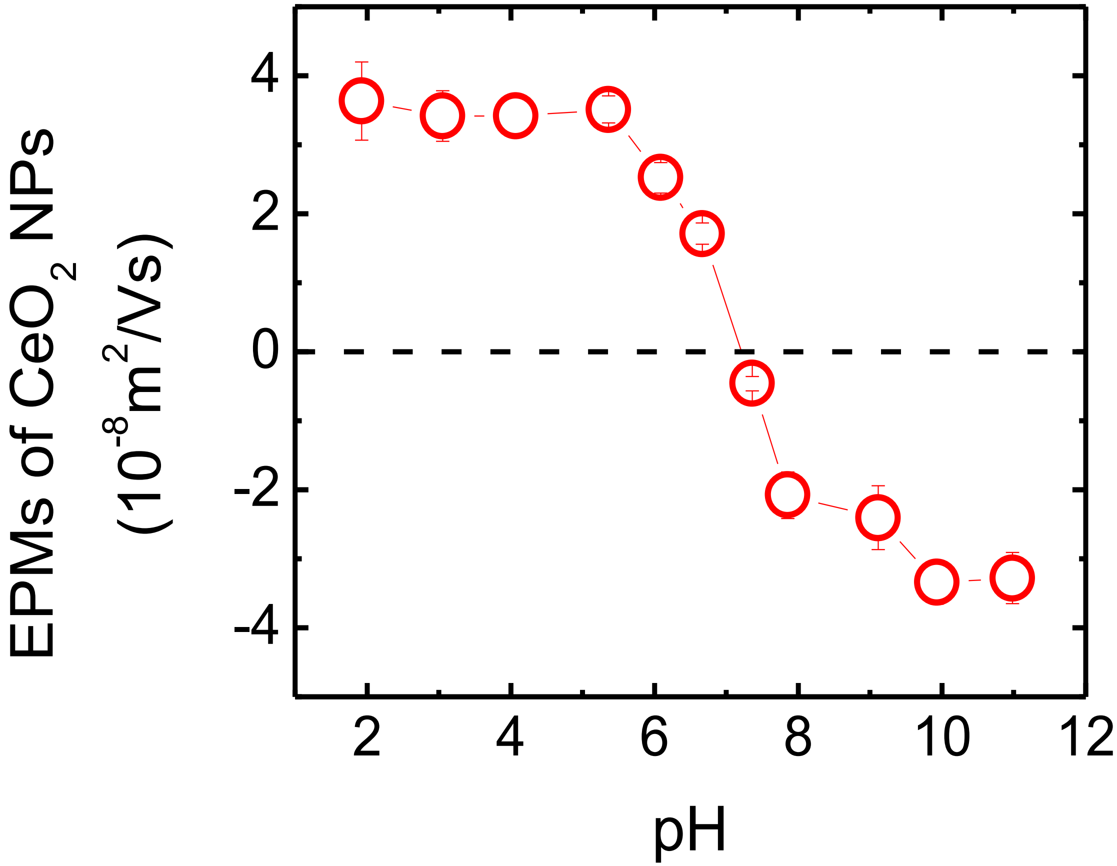
- **CeO_2 NPs were received from Professor Reyes Sierra's group at the University of Arizona**
- **Purchased from Sigma-Aldrich**
- **NPs were examined under TEM**
- **NPs are mostly angular**

Elemental Composition of CeO_2 NPs



- The elemental composition of the NPs were determined through energy dispersive X-ray spectroscopy (EDS)
- The NPs are largely composed of cerium and oxygen
- Trace amount of aluminum, silicon, and phosphorus is present

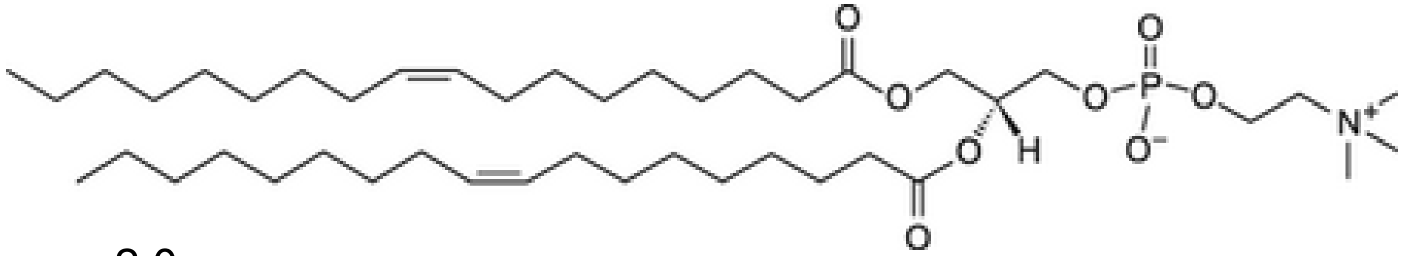
Electrokinetic Properties of CeO_2 NPs as a Function of Solution pH

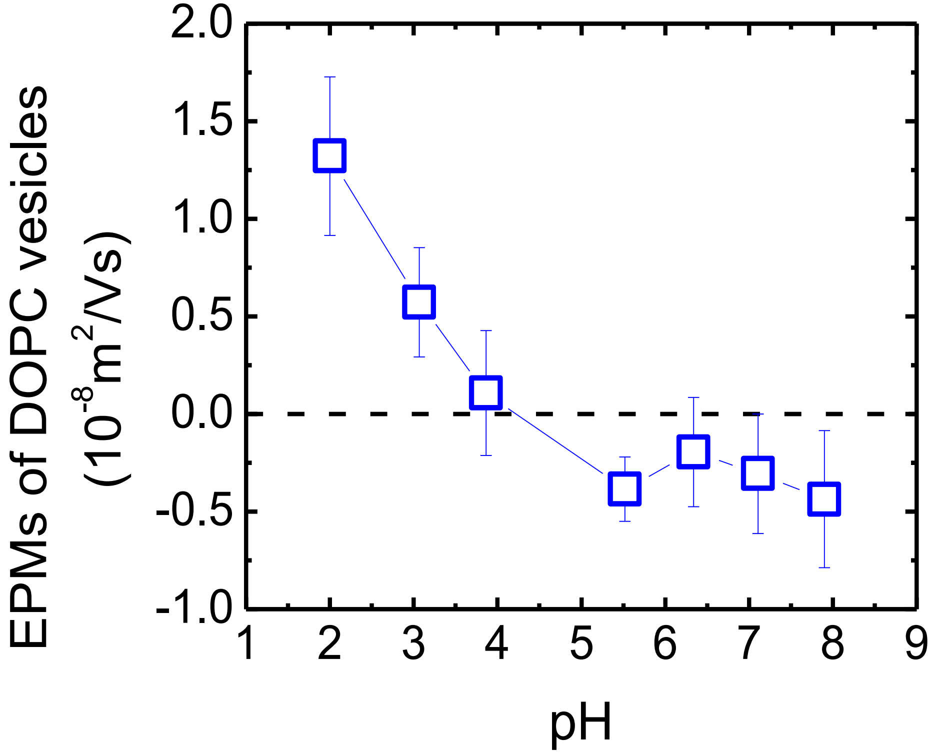


- **The pH of zero point of charge (pH_{ZPC}) of CeO_2 NPs is about 7**

DOPC Supported Lipid Bilayers (SLBs) as Model Cell Membranes

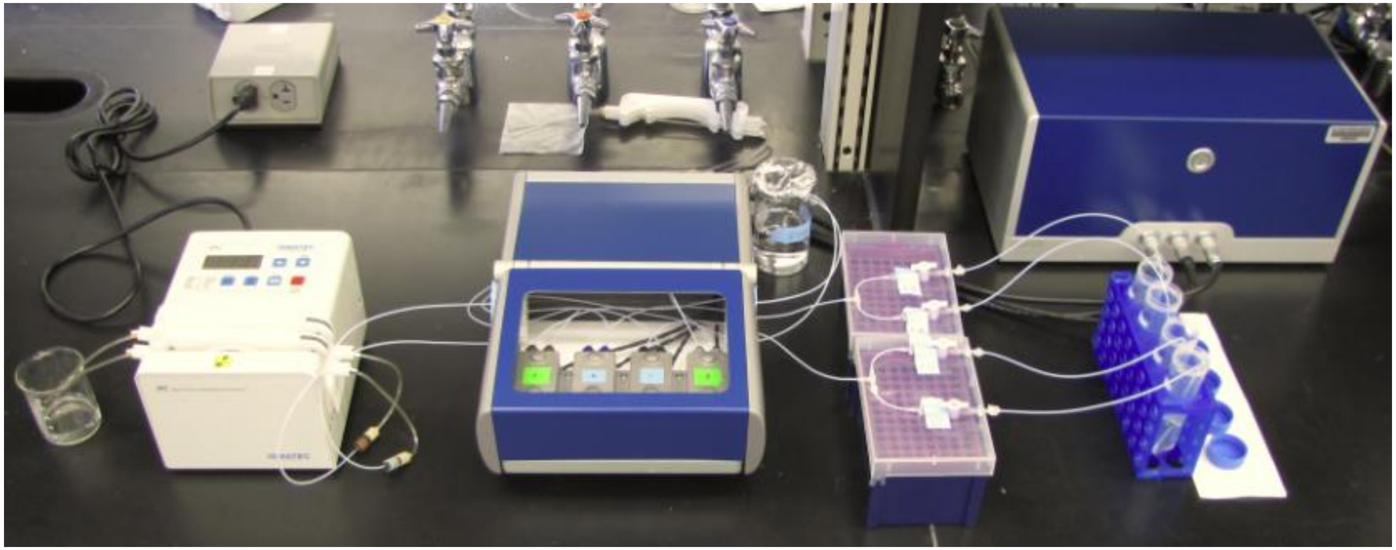
DOPC (1,2-dioleoyl-*sn*-glycero-3-phosphocholine)

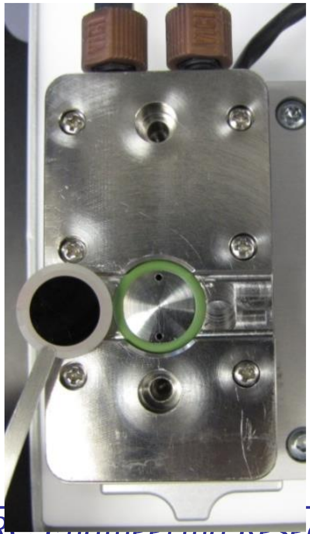


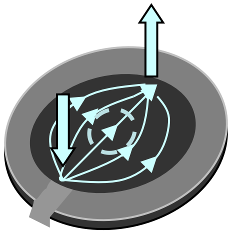


- **DOPC vesicles prepared by extrusion with 50-nm membranes**
- **pH_{ZPC} of DOPC is about 4**

Quartz Crystal Microbalance with Dissipation Monitoring (QCM-D)





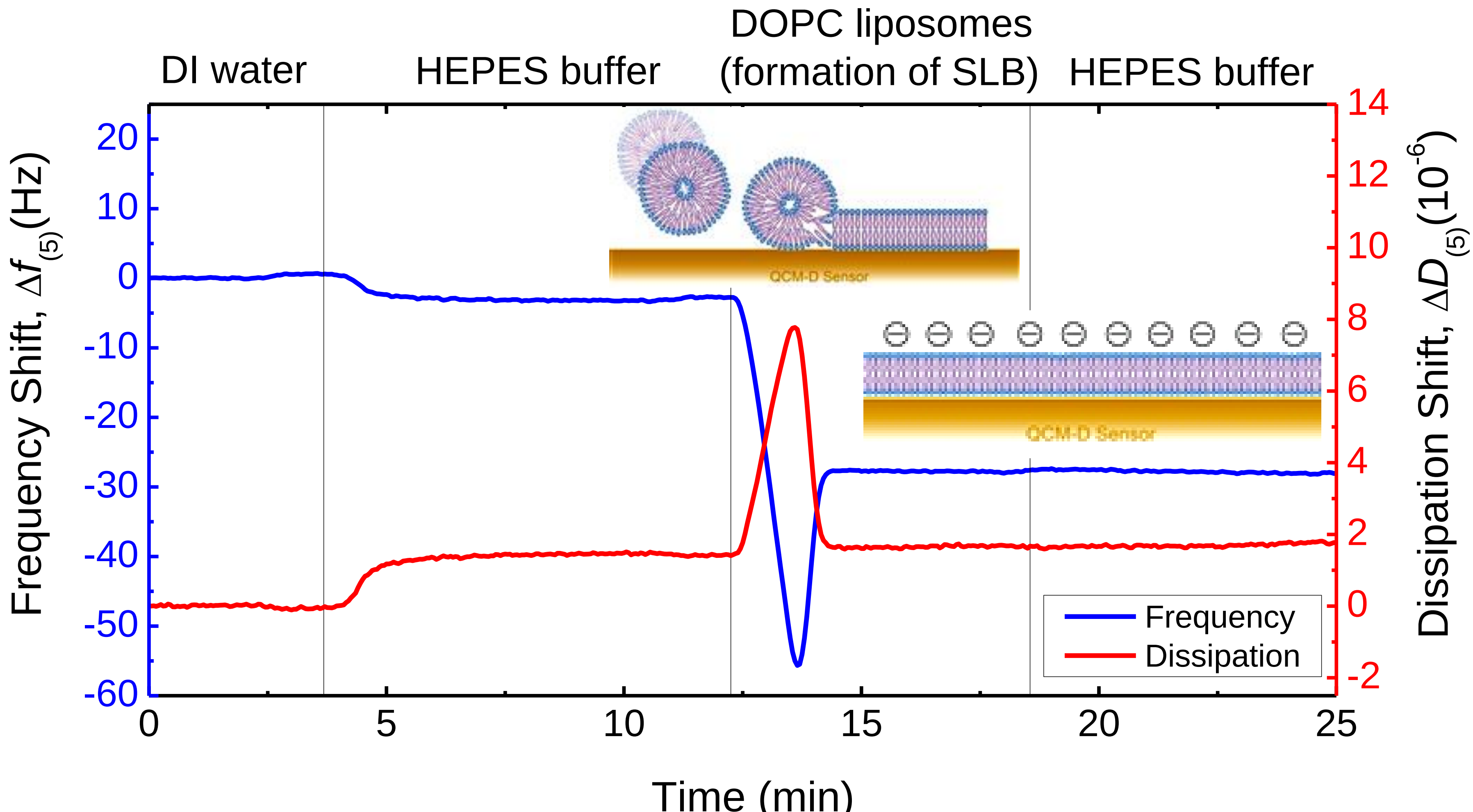


- **Sensitivity of ca. 10 ng/cm^2**
- **Frequency, Δ*f* – deposited mass**
- **Dissipation, Δ*D* – "softness" of deposited constituents**
- **Laminar flow at 0.1 mL/min**
- **T = 25 ºC, pH = 2–8**

Picture of crystal is from qsense http://www.qsense.com/

Formation of Supported Lipid Bilayers on Silica-Coated QCM-D Crystals

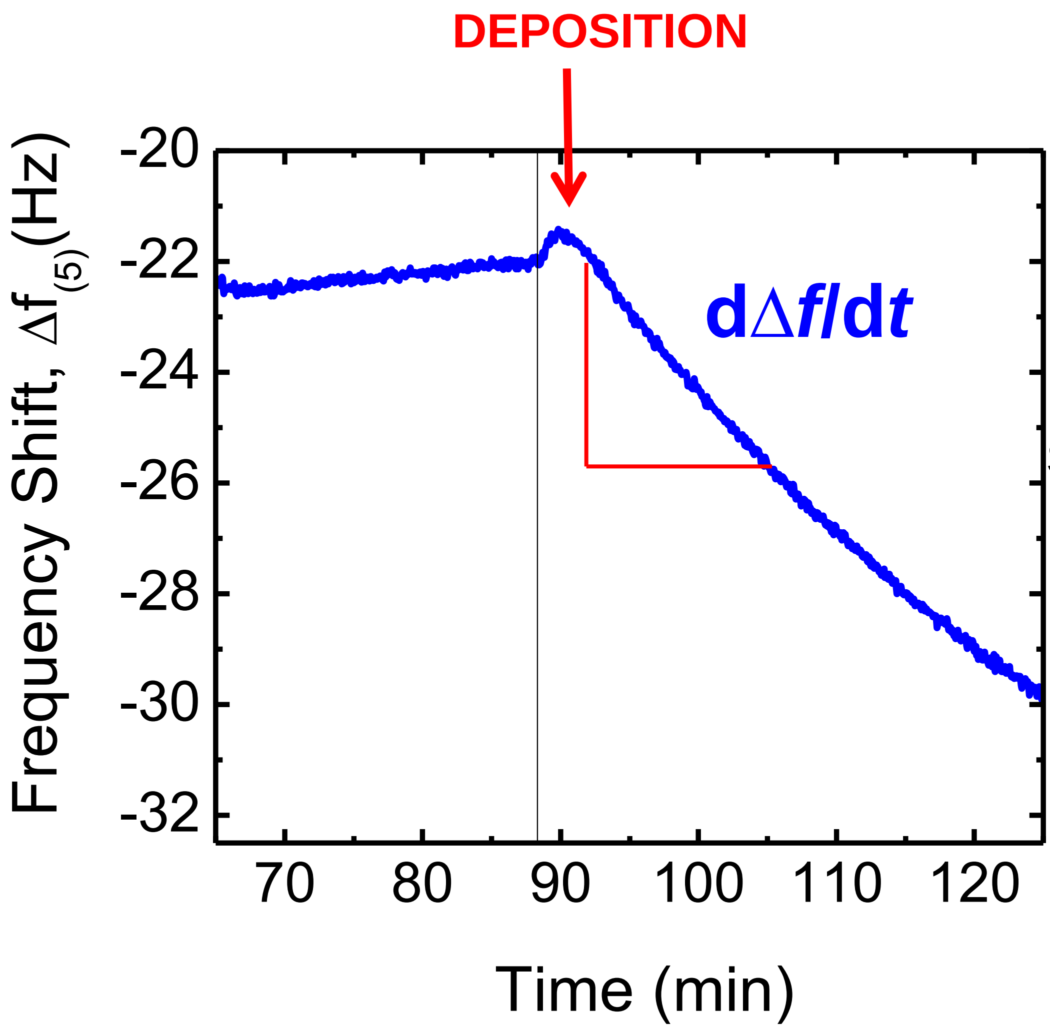
- **Approach of Keller and Kasemo, 1998**

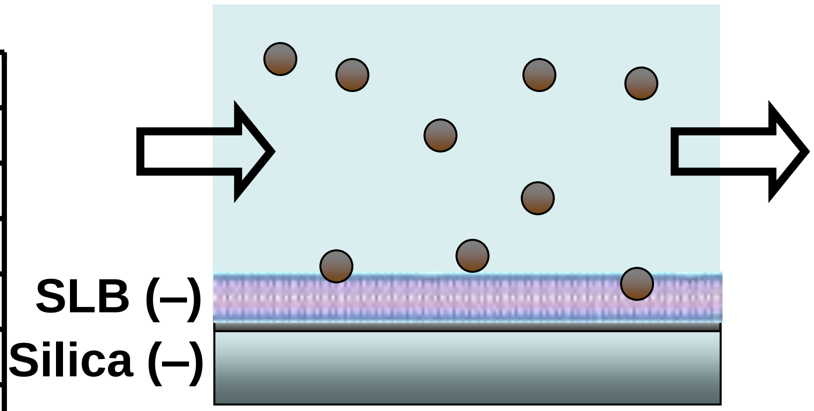


SRC Engineering Research Center for Environmentally Benign Semiconductor Manufacturing

Cartoons are from qsense http://www.qsense.com/

Deposition of CMP NPs on SLBs

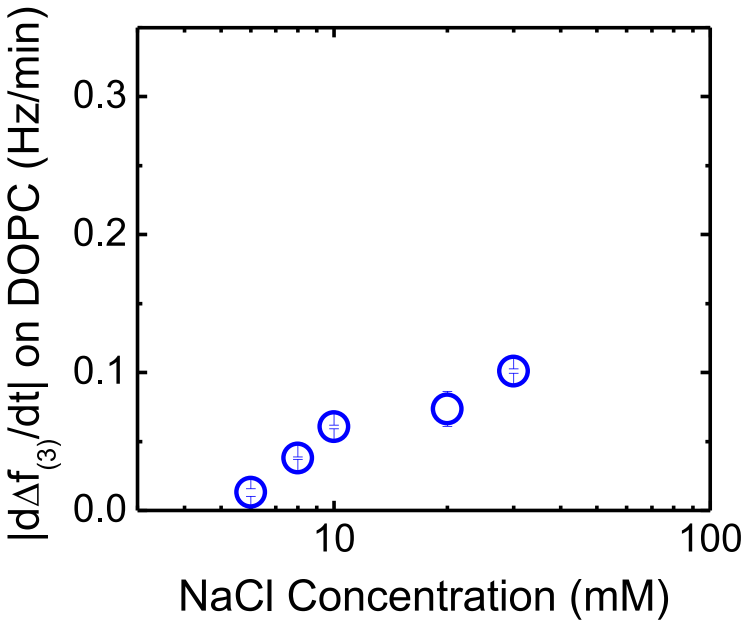




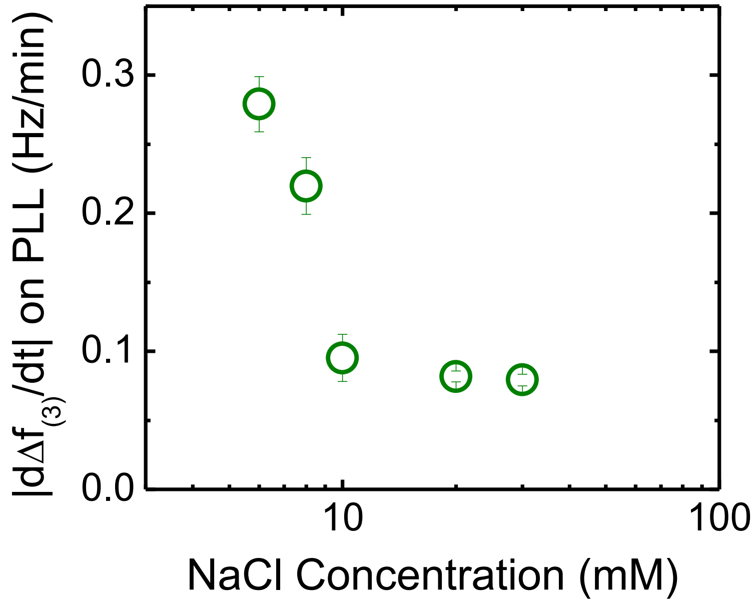
- **dΔf/dt is proportional to rate of nanoparticle deposition**

Deposition Kinetics of CeO_2 NPs on SLBs at pH 8.0

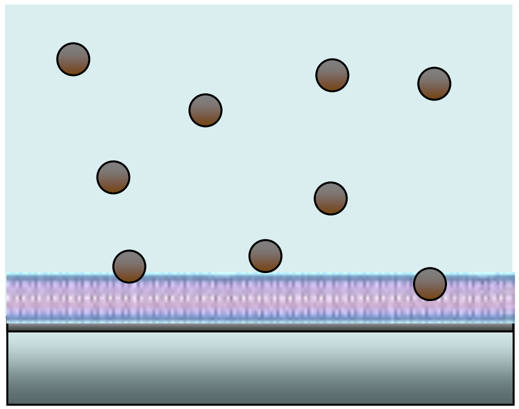
Deposition Rates on SLBs

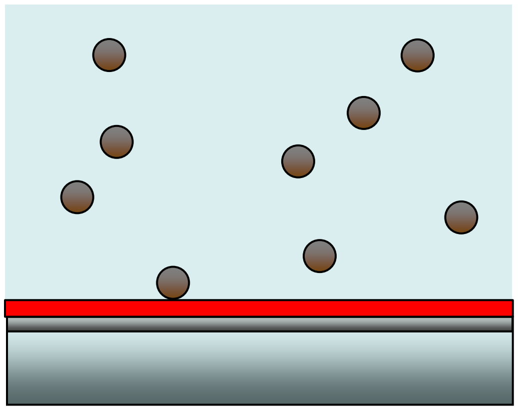


Favorable Deposition Rates on Poly-L-lysine (PLL) Layers



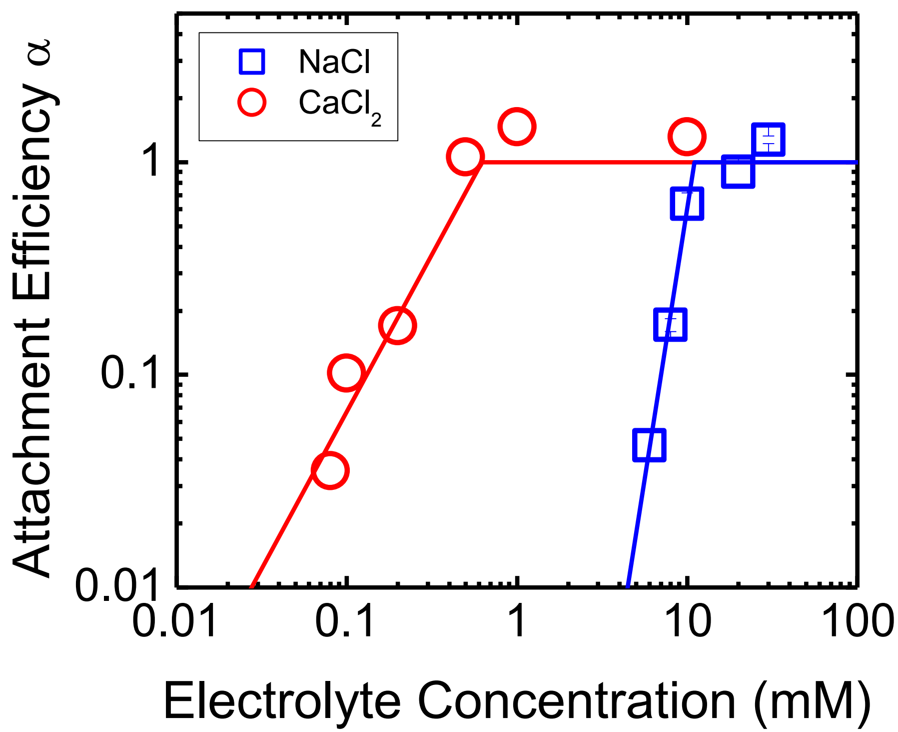
SLB





PLL Layer

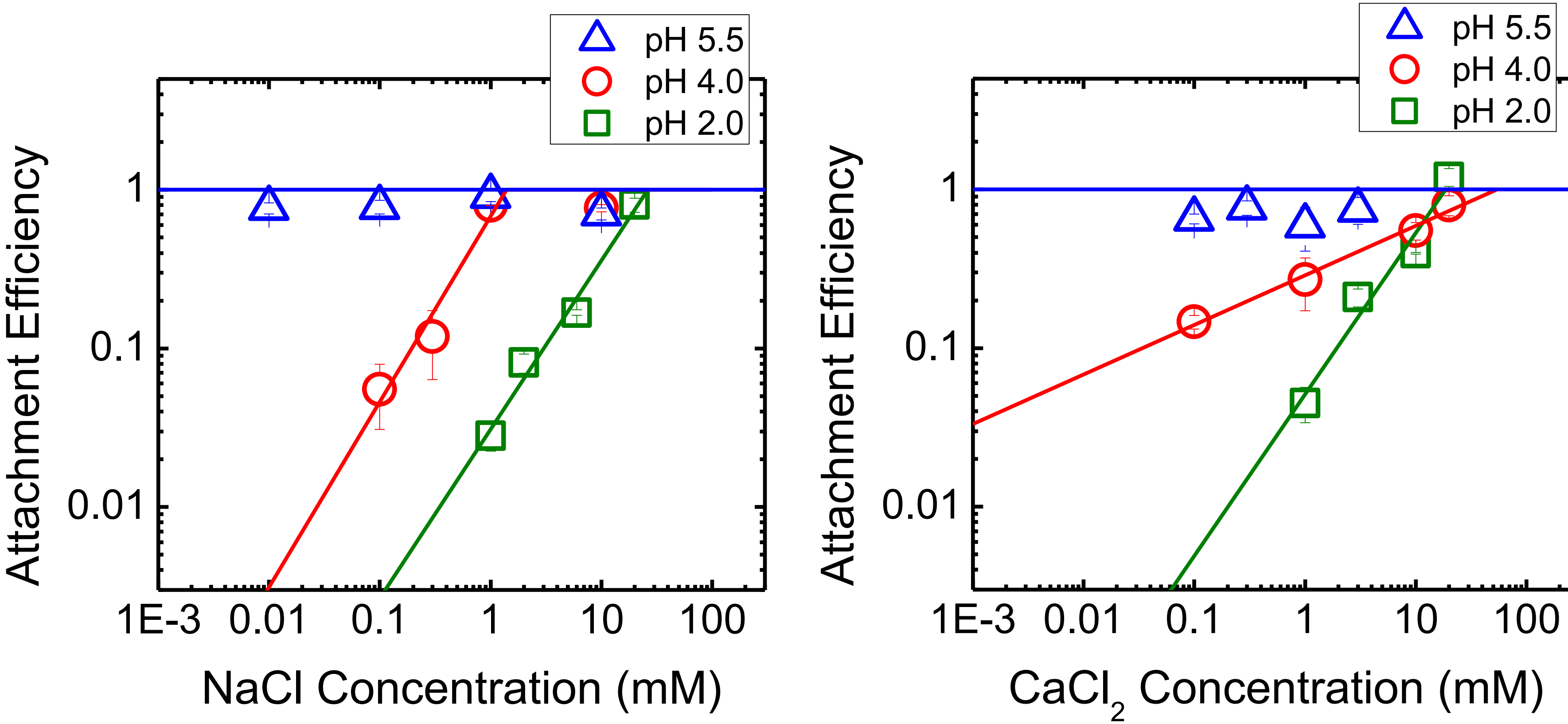
Deposition Kinetics of CeO_2 NPs on SLBs at pH 8.0



$$\alpha = \frac{d\Delta f / dt}{(d\Delta f / dt)_{favorable}}$$

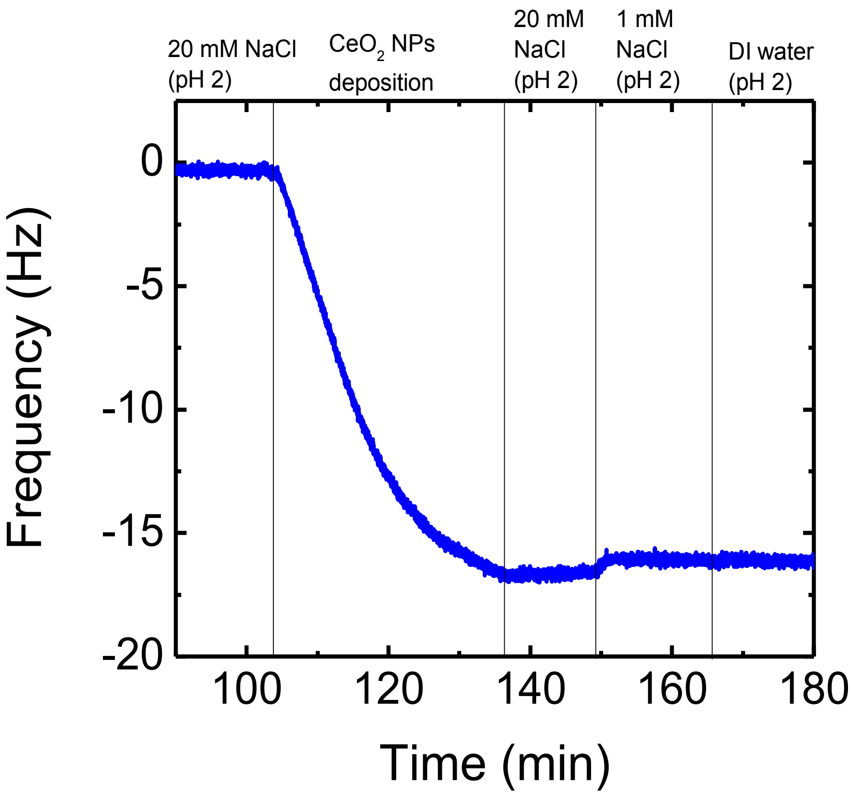
- **Deposition behavior on SLBs in NaCl and $CaCl_2$ is in qualitative agreement with classical DLVO theory**
- **Favorable deposition takes place at >10 mM NaCl at which sufficient charge screening takes place**
- **Favorable deposition takes place at >0.5 mM $CaCl_2$ where SLBs undergo charge reversal**

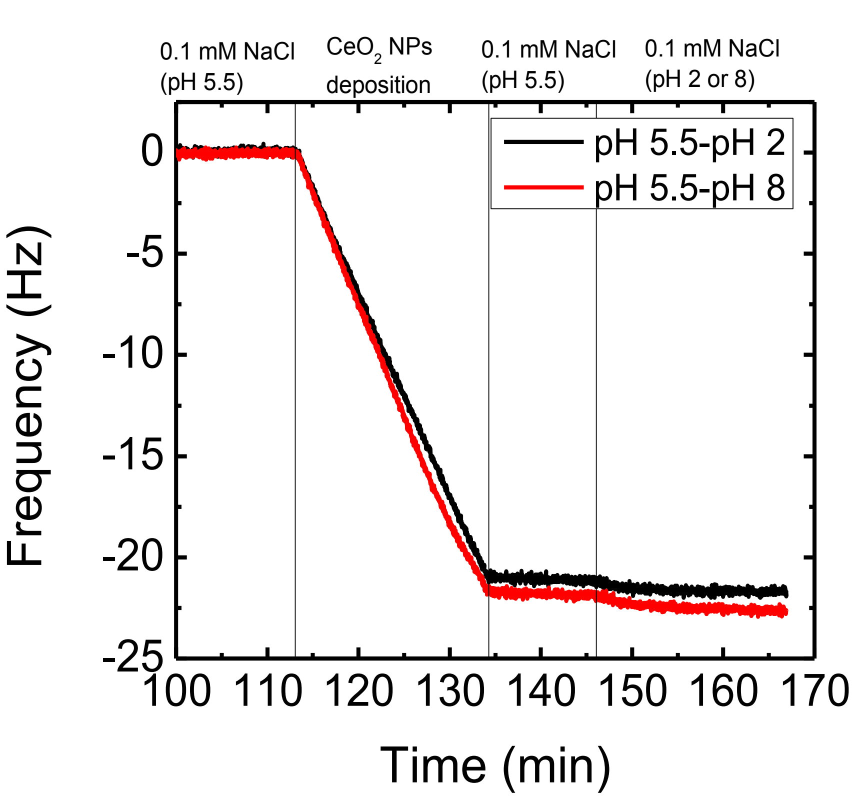
Deposition Kinetics of CeO_2 NPs on SLBs at pH 2.0, 4.0, and 5.5



- **At pH 2.0, both CeO_2 NPs and SLBs are positively charged**
- **At pH 4.0, CeO_2 NPs are positively charged and SLBs are slightly positively charged**
- **At pH 5.5, CeO_2 NPs are positively charged while SLBs are negatively charged**

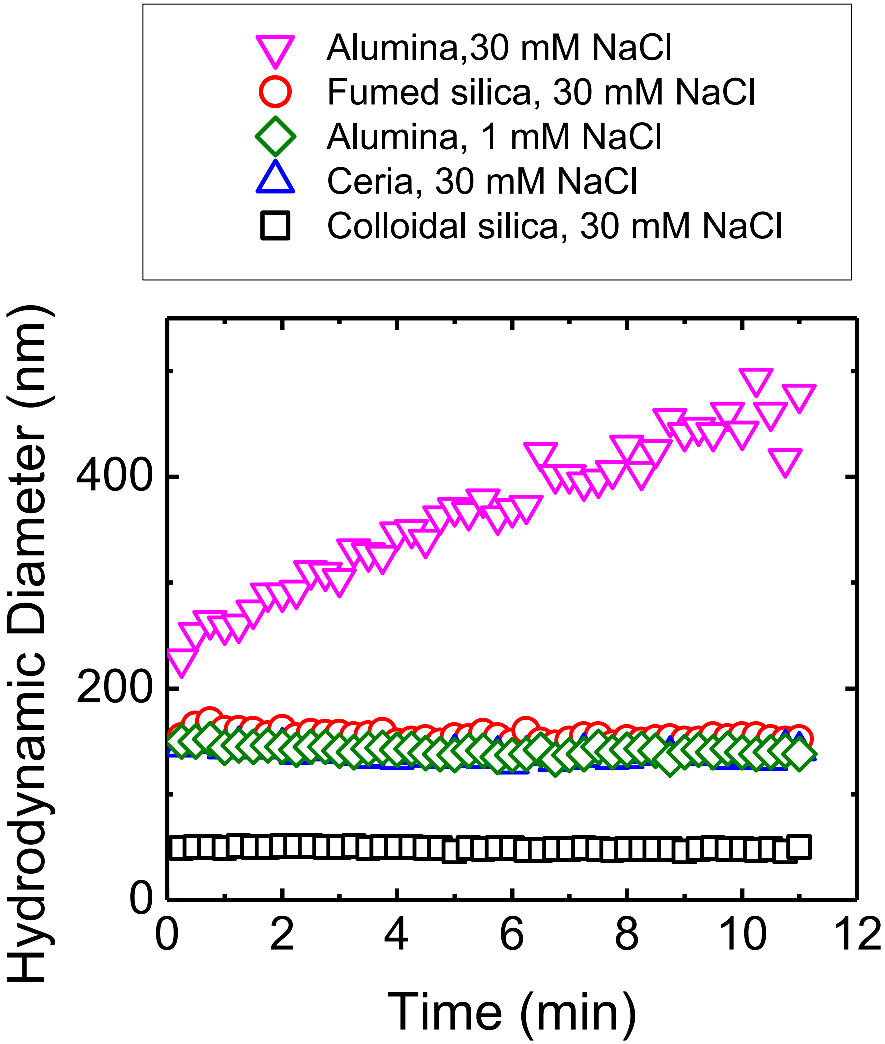
Reversibility of CeO_2 NP Deposition on SLBs





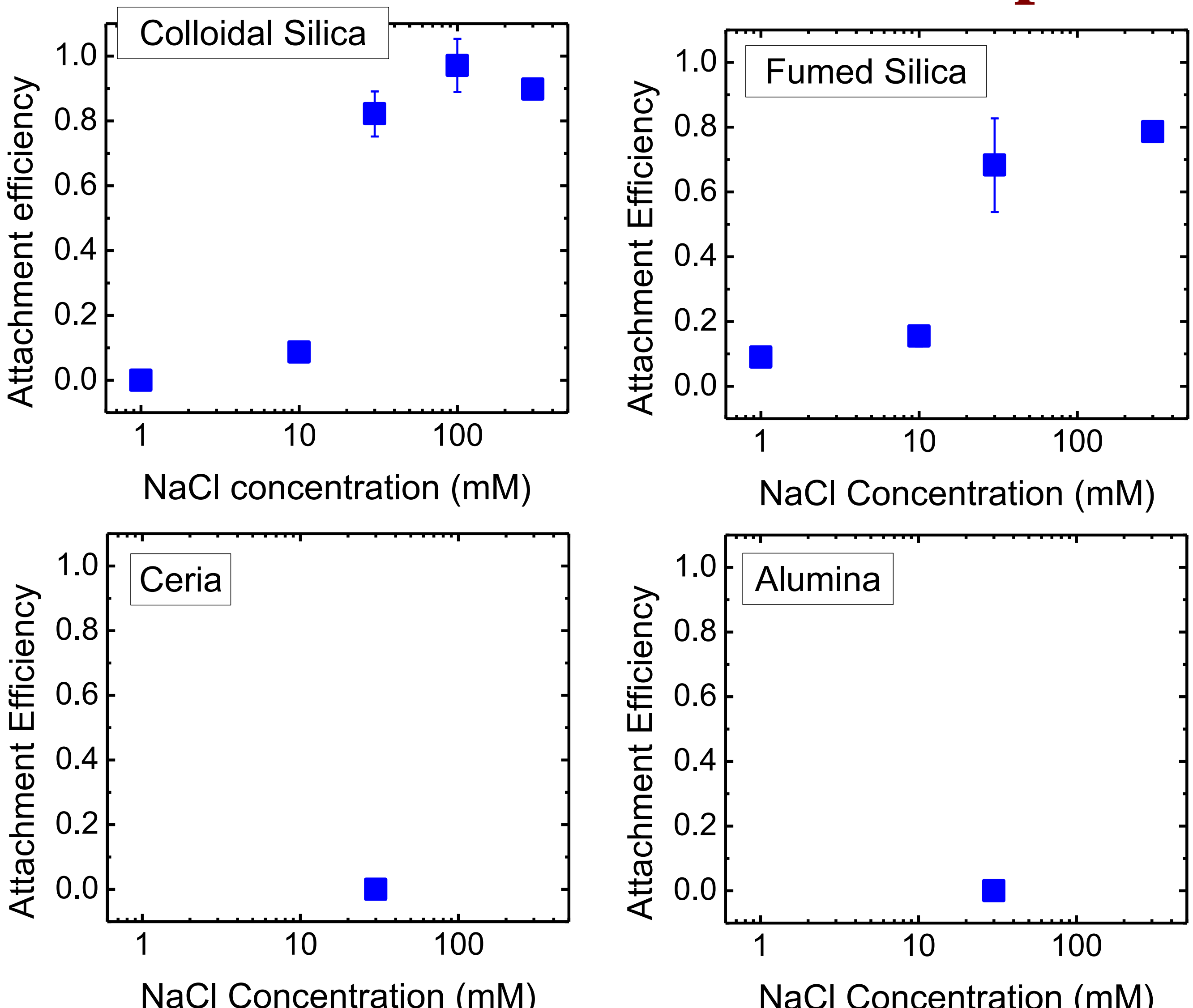
- **CeO_2 NPs deposition on SLBs is mostly irreversible**
- **Since the QCM-D only allows for NP deposition in the primary energy minimum, the depth of the minimum is too deep for the deposited NPs to escape**

Comparing Colloidal Stability of Cabot CMP NPs on SLBs at pH 7.4



- **Time-resolved dynamic light scattering (DLS)**
- **All CMP NPs from Cabot Microelectronics are stable to aggregation at 30 mM NaCl, except the aluminum oxide NPs**
- **Aluminum oxide NPs, however, are stable to aggregation at 1 mM NaCl**

Comparing Deposition Kinetics of Cabot CMP NPs on SLBs at pH 7.4



- **At pH 7.4, all CMP NPs are negatively charged**
- **For both silica NPs, deposition kinetics increases as NaCl concentration increases**
- **Ceria and alumina NPs have low propensity to attach to membranes**

Summary of Current Findings

- **Solution chemistry, such as ionic strength, counterion valence, and pH, play important roles in controlling the attachment of CMP NPs on model biological membranes.**
- **Surface charge properties of CMP NPs, as well as SLBs, are important considerations for NP–membrane interactions.**
- **Attachment of NPs is affected by the chemistry of SLBs. Ca^{2+} can reverse the charge of DOPC SLBs.**
- **The QCM-D is sensitive enough to measure the attachment of CMP NPs on model biological membranes. Small sample volumes (ca. 5 mL) are required. Thus, it has the potential to be used as an rapid or online assay for nanoparticle propensity to bind to membranes.**

Industrial Interactions and Technology Transfer

- **Dr. Chen, together with the other PIs from the SRC ERC, have obtained representative CMP NPs from Cabot Microelectronics in order to investigate their propensity to attach to biological membranes**
- **Dr. Chen, together with the other PIs, have closely interacted with SRC industrial members (David Speed from IBM and Mansour Moinpour from Intel) regarding research progress**
- **SRC industrial members will be updated on the development of the QCM-D as a rapid and online binding assay for nanomaterials**
- **SRC industrial members will be informed of the types of CMP NPs that have a strong propensity to bind to cell membranes based on the research findings in Dr. Chen's lab**
- **Dr. Chen's group presented 3 ERC/SRC teleseminars**

Future Plans

Next Year Plans

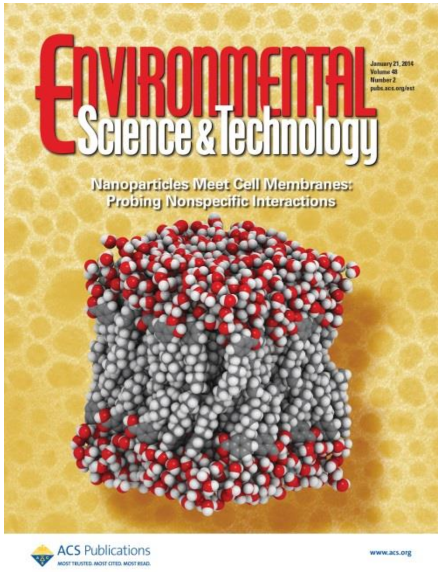
- Investigate the propensity of CMP NPs to penetrate or disrupt model biological membranes
- Develop a rapid assay using the QCM-D to evaluate the propensity of CMP NPs to disrupt biological membranes

Long-Term Plans

- Examine the interactions of aged and transformed CMP NPs after being employed for polishing with model biological membranes
- Increase the complexity of model biological membranes through the consideration of mixed-lipid membranes and the incorporation of proteins in bilayers

Publications, Presentations, and Recognitions/Awards

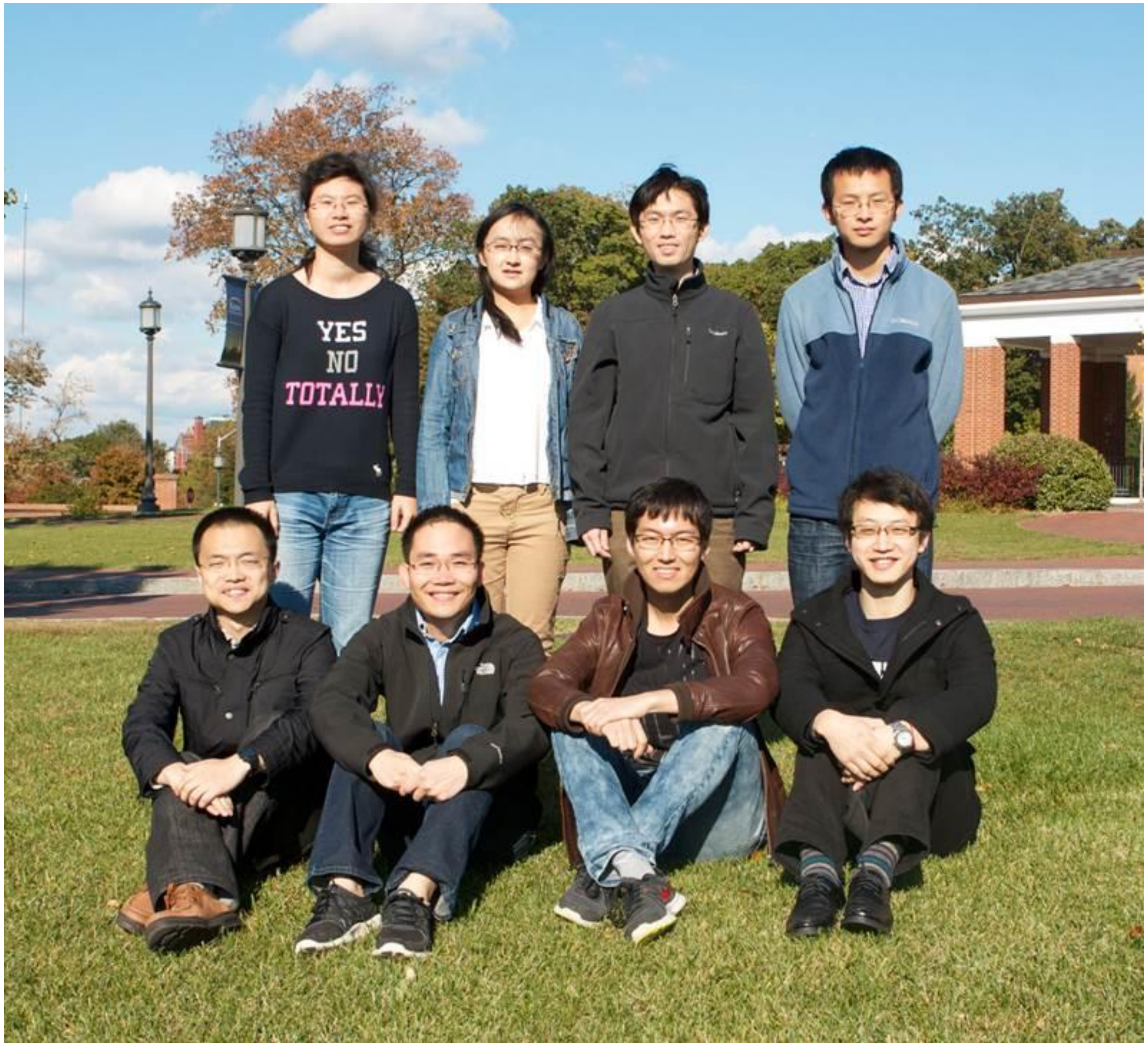
- **Publications**
  - **Four papers have been accepted by/published in *Environmental Science & Technology*, including a feature article featured on the cover of *ES&T***
  - **Two other manuscripts have been submitted**
- **Presentations**
  - **Dr. Chen has been invited to give talks at Washington University in St. Louis, Tsinghua University (China), ACS Meeting at San Francisco, and US Environmental Protection Agency**
  - **3 oral presentations**



Publications, Presentations, and Recognitions/Awards

- **Recognitions/Awards**
  - **Dr. Chen was invited to give a keynote talk at the International Water Association (IWA) Symposium on Environmental Nanotechnology in Nanjing, China**
  - **Peng Yi received one of the prestigious 2013 C. Ellen Gonter Environmental Chemistry Awards from the American Chemical Society Division of Environmental Chemistry**
  - **Khanh An Huynh recently received one of the prestigious 2014 C. Ellen Gonter Environmental Chemistry Awards**
- **Students**
  - **2 Ph.D. students graduated: Peng Yi (2013) and Khanh An Huynh (2014)**
  - **1 MSE student graduated: Wenyu Gu (2013)**

Thank you!



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